UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,424	04/13/2001	Stuart L. Schreiber	331D USD1	5917

7590 11/02/2004

Brenda Herschbach Jarrell, Ph.D, Choate, Hall
& Stewart, Exchange Place,
53 State Street
Boston, MA 02109

EXAMINER	
VOGEL, NANCY S.	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/834,424	SCHREIBER ET AL..FR	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 8-29 are pending in the case.

In view of the appeal brief filed on 7/26/04, PROSECUTION IS HEREBY REOPENED. A new ground of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is based on the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, first paragraph "Written Description"

Requirement published in the Federal Register (Volume 66, Number 4, pages 1099-1111). Claim 8 is drawn to a method for preparing an agent that effects a biological event mediated by the association of two or more endogenous cell surface receptors, the method comprising preparing said agent which includes a first non-peptidic moiety that binds to one of the cell surface receptors covalently linked to a second non-peptide moiety that binds to the other cell surface receptor, wherein the agent binds to both cell surface receptors. Claim 19 is drawn to a method for preparing an agent that effects a biological event mediated by the association of two or more endogenous protein mediators, the method comprising preparing an agent which includes a first non-peptide moiety that binds to one of the protein mediators covalently linked with a second non-peptide moiety that binds to the other protein mediator, wherein the agent binds to both protein mediators, the biological event is mediated by the association of molecules of two different protein mediators and the first and second moieties are different. These are genus claims in terms of any methods of preparing any agent made up of two non-peptidic moieties that has the ability to bind two cell surface receptors (claims 8-18) or two endogenous protein mediators (claims 19-29) in order to effect a biological event.

The specification specifically mentions several possible agents such as immunophilins (i.e. FK506 or rapamycin) and other ligands that bind to a receptor or binding partner, and further state that "other compounds capable of binding to those receptors or to other endogenous constituents may be readily identified using a variety of approaches" (page 14, lines 12-13 of the specification). None of these moieties have been shown, when combined with a second non-peptidic moiety, to effect a biological

event, and therefore it is unclear that these "dimerizers" will serve to actually activate a signal transduction/biological event by dimerizing their targets. Thus, there is no description of even a single compound that is comprised of two non-peptidic moieties that each bind to a cell surface receptor, or endogenous protein mediator, where the agent can effect a biological event mediated by the association of the two receptors or endogenous protein mediators. Therefore, the description provided by the specification is not deemed to be descriptive of a structure-function relationship of a representative number of species that are encompassed by the claims. This is because the skilled artisan cannot envision a sufficient number of agents which include two non-peptide moieties that bind to cell surface receptors or endogenous protein mediators, wherein the compounds have the ability to effect a biological event mediated by the association of the two cell surface receptors or endogenous protein mediators. There is no description of a structural feature that correlates with the functional ability of an agent to bind two cell surface receptors, or two endogenous protein mediators in a manner which results in an effect on a biological event mediated by the association of said receptors or endogenous protein mediators. Irrespective of the fact that such disclosed agents as immunophilin-based agents are questionable with respect to their functionality in the claimed invention, there is not even a disclosure that the immunophilin-based agents are representative of all agents within the genus of compounds that are effective to bind to two receptors or endogenous protein mediators in a manner effective to elicit an effect on a biological event. As a result, the instant specification does not describe the method for preparing agents which effect a biological event in such a clear and concise

manner so as to indicate that the appellant had possession of these agents at the time of filing of the application. Thus the written description requirement has not been satisfied.

Applicant's arguments set forth in the Appeal Brief filed 7/26/04 have been considered but have not been found convincing.

Applicant has argued that the specification discloses that the invention encompasses methods for preparing any dimerizer that includes two covalently linked non-peptide moieties each of which binds to the same or a different protein mediator such as a cell surface receptor, as required to describe the broadest of the claims, and points to various portions of the specification which are alleged to support the written description of these molecules. The portions of the specification which are specifically mentioned include pages 11-12, in which statements are made of the desirable characteristics of dimerizers, including binding affinity, ability to transport membranes, and physiological acceptability. The applicant also points to portions of the specification which contain listings of receptors for which dimerizers are desirable (page 8-11). Applicants further argue that the skilled artisan would have found it trivial to provide or identify moieties that bind to a protein. Applicants further argue that post-filing research (Qureshi and Tian) has produced agents that meet the functional limitations of binding to two proteins and served to activate a biological pathway. Applicants further argue that "an overly rigid request for structure disclosure misses the mark" and that the written description standard of the Examiner would "require Appellant to include a picture or name of every chemical entity that binds an endogenous protein mediator and

could be included in a dimerizer for use in accordance with the present invention" (page 5). However, it is maintained that the assertion that any appropriate agent can be made in the claimed method does not establish a structure-function relationship between the agent and the protein that it binds and regulates, which is the standard for Written Description. The Office has adequately established that the specification provides no correlation between a particular structure of any agent and its functional ability to oligomerize and activate a receptor. As such, the skilled artisan cannot envision which agents can be used to oligomerize any given protein mediator in order to activate a particular signal transduction cascade. The fact that the skilled artisan cannot ascertain which agents will provide the necessary function alone establishes that the Written Description requirement has not been met. It is noted that Applicant cannot rely on post-filing art to satisfy the requirements of 35 USC 112, first paragraph if that post-filing art does not itself rely on the specification at issue. In the instant case, the teachings of Qureshi and Tian do not rely on the instant specification because the oligomerizing agents taught in those references are not disclosed in the instant specification. This also establishes that Applicant has not described the broad genus of agents to be used in their invention because the agents used by Qureshi and Tain are not described or contemplated in terms of a structure-function relationship with regard to the instant invention.

The agents provided in the instant specification, i.e. FK506 dimers and related molecules, all relate back to immunophilin-receptor oligomerizing agents; this is not commensurate in scope with the broad genus of agents that are indicated to be used in

the claimed methods. Furthermore, it is noted that the agents described in the specification bear no structural or functional relationship to the agents discovered by Qureshi and Tian; thus the skilled artisan could in no way envision the use of those agents in the claimed method based upon the teachings of the instant specification. Therefore this again establishes a lack of written description.

Describing a structure-function relationship is the nature of Written Description, thus the Office action is not being overly rigid but rather applying the appropriate standards. It is not simply enough to say that an agent must bind to the receptor it is designed to oligomerize in order to establish a structure-function relationship. There must be a particular structure(s) that is disclosed to bind to a particular receptor-type such that the skilled artisan could envision that agents having the structure(s) could be used to oligomerized the particular receptor-type, thereby effecting a biological function. The wish or desire to isolate appropriate binding moieties is not sufficient.

For the above reasons, the rejection is maintained.

It is noted that this Office action contains rejections of the same claims under 35 USC 112, 1st paragraph (written description) and 35 USC 102(b). While these rejections may seem contradictory, they are not because each is based upon a different legal analysis, i.e. sufficiency of the disclosure of the instant application to support claims under 35 USC 112 1st paragraph vs. sufficiency of a prior art disclosure to anticipate or render obvious an embodiment(s) of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Wold (Methods in Enzymology Vol. 11, pages 617-640, 1966).

Wold disclose methods of preparing agents comprising preparing an agent which includes a first non-peptidic moiety that binds to one cell surface receptor covalently linked to a second non-peptide moiety that binds to the other cell surface receptor, wherein the agent binds to both cell surface receptors (see page 618, lines 17-28; see pages 622 line 34 – page 640). The two moieties may be the same or different (see page 618, last paragraph). The reference discloses the method of preparing bifunctional reagents whose molecular weight of the first and second non-peptide moieties are less than 5 Kd (see for example page 623, 625, 627). In the absence of evidence to the contrary, the agents disclosed by Wold would bind to any two proteins, including cell surface receptors, or two endogenous protein mediators, which are in physical proximity, thereby effecting a biological function.

Claims 8-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Ji et al. (Methods in Enzymology, Vol. 91, pages 580-609, 1983).

Ji et al. disclose methods of preparing agents comprising preparing an agent which includes a first non-peptidic moiety that binds to one cell surface receptor covalently linked to a second non-peptide moiety that binds to the other cell surface receptor, wherein the agent binds to both cell surface receptors, including such agents as formaldehyde and gluteraldehyde, which form polymeric forms in solution and which bind and cross-link membrane proteins or other proteins nonspecifically (see page 601-602). The reference discloses formaldehyde and gluteraldehyde in aqueous solutions (see page 602). The reference discloses preparation of bifunctional reagents, having two different moieties which each can bind to any protein of interest (see page 584, second complete paragraph through page 601). The reference discloses the method of preparing bifunctional reagents whose molecular weight of the first and second non-peptide moieties are less than 5 Kd (see for example pages 591 and 592). In the absence of evidence to the contrary, it is considered that the agents disclosed by Ji would bind to any two proteins, including cell surface receptors, or two endogenous protein mediators, which are in physical proximity, thereby effecting a biological function.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DAVID GUZO
PRIMARY EXAMINER

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600